REMARKS/ARGUMENTS

I. Status of the Claims

Claims 1-29 were initially filed. As a result of a restriction requirement, claims 9-12, 14, 22, 23, and 27-29 have been withdrawn. New claims 30 and 31 are added in the present amendment. Upon entry of the amendment, claims 1-3, 6-8, 13, 15-21, 24-26, 30, and 31 are under examination.

Claim 1 is amended to recite sequence identifiers and functional limitations from claim 5. The recitation from claim 5 is amended to begin parts (a) to (j) with the same part of speech, as well as to correct a typographic error. The phrase "meristem size and/or activity" can be found in lines 30-31 of page 10. Claims 4 and 5 are canceled for redundancy. Claims 13, 15, and 24 are amended to recite sequence identifiers and to ensure proper antecedent basis and recite functional limitations from claim 5. Claim 7 is amended to recite "the polynucleotide sequence" for proper antecedent basis. Claims 13 and 25 are amended to correct improper use of articles. Support for new claims 30-33 can be found throughout the specification, and particularly in claims 1, 13, 15, and 24 as originally filed. The specification is amended to comply with the Examiner's request for a more descriptive title and abstract, to delete a hyperlink, and further to eliminate erroneous description of the locations of DMT Domains A and B in SEQ ID NO:2. The correct description is on page 13, lines 3-6. The full name *DEMETER* for DMT can be found in line 12 on page 21 of the specification. The present amendment introduces no new matter.

II. Objections

A. Hyperlink

The Examiner objected to the specification for an embedded hyperlink. The present amendment has deleted the hyperlink.

B. Title and Abstract

The Examiner also objected to the title and abstract of the disclosure, alleging they are not descriptive of the claimed invention. In response, Applicants have submitted an

amended title and an amended abstract. Should the Examiner find the title or abstract as amended still unsatisfactory, Applicants request that the Examiner suggest specific language that would be acceptable.

C. Missing Sequence Identifiers in Claim 1

The Examiner also objected to claim 1 for missing sequence identifiers. Claim 1 as amended now recites sequence identifiers.

D. "Modulate" in Claim 5

The word "modulate" in claim 5 was further objected for incorrect usage. Claim 5 has been canceled and thereby renders the objection moot.

E. Improper Articles in Claims 18 and 25

In addition, the Examiner objected to claims 18 and 25 for improper use of articles. The present amendment has addressed the issue.

III. Rejections

A. 35 U.S.C. §101

Claims 1, 4, 7, 8, 13, 15-20, and 24, and 25 were rejected under 35 U.S.C. §101 for alleged lack of a specific asserted utility or a well-established utility. Specifically, the Examiner pointed to EMBL Accession No. Q94LX6 (Asada et al.), which is a nucleic acid encoding a prenyltransferase with at least 60% identity to SEQ ID NO:72. As this nucleic acid appeared to be within the claimed subject matter and the specification has asserted no utility of prenyltransferase, the Examiner concluded that the claimed invention lacks utility.

Applicants respectfully note that Q94LX6 is not within the genus of nucleic acids encompassed by the amended claims. Moreover, a specific utility for the present invention is asserted in the instant disclosure, *e.g.*, on page 21 line 23 to page 22 line 9. As such, Applicants submit that the rejection for lack of utility should be withdrawn.

B. 35 U.S.C. §112 First Paragraph

1. Enablement

The Examiner rejected claims 1, 2, 4, 7, 8, 13, 15-21, and 24-26 under 35 U.S.C. §112 first paragraph as not properly enabled. Specifically, the Examiner stated that since the claimed invention has no well established utility or specific asserted utility, one of skill in the art would not know how to use the invention. As discussed above, the instant application does assert a specific utility. Applicants thus submit that the enablement rejection on this ground should be withdrawn.

The Examiner also held the claimed invention not fully enabled in view of claim scope and the teaching of the present application. Specifically, the Examiner stated that the pending claims are drawn to a broad genus of nucleic acids encoding polypeptides with 40% identity to at least one of SEQ ID NOs:71, 72, and 73, and that the specification does not teach how to obtain claimed nucleic acids other than SEQ ID NO:1 or 5. Citing some references where conservative substitutions were reported to significantly affect a protein's biological activity whereas non-conservative substitutions had no effect on protein function, the Examiner dismissed the teaching of making conservative substitutions in the present application as useful guidance for one of skill in the art to practice the claimed invention (bridging paragraph between pages 6 and 7 of the December 26, 2002, Office Action). The Examiner also regarded the asserted functions of polypeptides encoded by the claimed nucleic acids as unreliable speculation based on sequence homology to proteins of known functions (first full paragraph on page 8 of the Action). It was further alleged that the specification does not teach methods for assaying protein functions as enumerated in claim 5 or methods for transforming plant cells with claimed nucleic acids (bridging paragraph between pages 8 and 9 and first full paragraph on page 9). The Examiner concluded that undue experimentation would be necessary for one skilled in the art to practice the claimed invention.

To establish a *prima facie* case of non-enablement, the Examiner must show that undue experimentation would be required to make and use the claimed invention. Moreover, as explained by the Court of Customs and Patent Appeals, "it is not necessary that a patent

applicant test all the embodiments of his invention." *In re Angstadt*, 190 USPQ 214, 218 (C.C.P.A. 1976). Some degree of experimentation is appropriate and acceptable under U.S. patent law. Even if the practice of the claimed invention requires a considerable amount of experimentation, it is not necessarily "undue" experimentation:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988) (citing *In re Angstadt*, 190 USPQ 214 (CCPA 1976). MPEP § 2164.06.

The pending claims are directed to nucleic acids comprising a polynucleotide sequence, or complement thereof, encoding a polypeptide comprising SEQ ID NO:71, 72, or 73 and having at least one of the specified biological activities. The experimentation necessary to identify a working embodiment of the present invention is not undue. The specification teaches both structural and functional characteristics of *DMT* nucleic acids and polypeptides sufficient for one of skill in the art to identify functional *DMT* sequences. The size, structure, and function of *DMT* polynucleotides are taught in the specification. Specific structural features of DMT polypeptides include at least one of the consensus sequences of SEQ ID NOs:71, 72, and 73, which correspond to defined segments of SEQ ID NO:2. *See, e.g.*, page 13 lines 3-6 of the specification.

In addition to the consensus sequences, the application also indicates that DMT polypeptides can comprise a bipartite nuclear localization signal, a leucine zipper sequence, and a generally basic region. *See, e.g.*, page 13 lines 14-26 of the specification. Moreover, the specification teaches that DMT polypeptides may contain a conserved HhH-GPD motif, including two alpha-helices and catalytic lysine and aspartic acid residues. *See, e.g.*, the bridging paragraph between pages 13 and 14. The function of DMT polypeptides is also described throughout the specification. For instance, *DMT* genes are involved in controling seed development and DNA methylation in a cell. *See, e.g.*, page 25 line 17 to page 26 line 8 of the

specification. Thus both the structural and functional features of *DMT* polynucleotides are provided in the specification.

At most, routine experimentation may be required to identify additional working embodiments within the scope of the claims. Polynucleotide sequences within the scope of the claims, such as natural variants of *DMT* nucleic acids comprising the consensus sequence of SEQ ID NO:71, 72, or 73, can be identified using the BLAST algorithm (page 17 line 19 to page 18 line 13). Indeed, SEQ ID NOs:1-70 represent specific sequences within the scope of the claims from a number of plant species. Candidate sequences obtained using well known molecular techniques to genetically alter sequences exemplified in the specification can also be generated and tested for activity.

The general strategy for making variants of the exemplary nucleic acids is disclosed in the specification. For instance, there is detailed disclosure from page 18 line 14 to page 20 line 31 and from page 36 line 26 to page 37 line 26 relating to how to make variants of the claimed nucleic acids. Such disclosure, in combination with the knowledge and techniques commonly known to those of skill in the relevant art, sufficiently enables one ordinarily skilled artisan to practice the present invention. With regard to the references the Examiner cited as evidence that protein functions may not always be preserved by conservative substitutions and non-conservative substitutions may not alter protein function, Applicants contend that even though the principle of generating protein variants by conservative substitution is not without exception, it is still a principle generally relied upon by skilled artisans. Thus, the discussion of conservative substitution as a means of making variants of the exemplary nucleic acids does provide significant enablement value.

Basic molecular techniques that are taught in the present application can be used to identify functional polynucleotide sequences. For example, standard laboratory procedures such as plant transformation (*see, e.g.*, page 35 line 5 to page 36 line 24) can be used to identify polynucleotide sequences within the scope of the claim that result in plants with any of the phenotypes (such as altered gene transcription and seed development) associated with *DMT*.

Changes in chromosomal methylation can be detected various known methods. *See, e.g.*, page 14 lines 26-33.

The Examiner alleged that undue experimentation would be required for one to practice the claimed invention because "[m]aking all possible single amino acid substitutions in an 1729 amino acid long protein...would require making and analyzing 19^{1729} nucleic acids." Applicants cannot agree with such reasoning. First of all, the claims as amended recite a polypeptide comprising at least one of SEQ ID NO:71, 72, or 73. Thus, a large number of residues within the consensus sequences (SEQ ID NO:71, 72, or 73) are explicitly defined.

Moreover, those skilled in the art would not substitute the non-conserved residues either within the consensus sequences or flanking the consensus sequences entirely randomly. The present specification provides numerous examples of *DMT* nucleic acids found in various species (such as barley, wheat, soybean, cotton, etc.). These naturally occurring *DMT* sequences provide important guidance for one skilled in the art to choose an amino acid for any non-conserved position in a candidate sequence with a reasonable chance that this sequence will encode a functional DMT polypeptide. As such, the amount of experimentation necessary for practicing the claimed invention in light of the present disclosure does not come close to that described by the Examiner.

The Examiner has not indicated how any of the above-described procedures are anything but routine. Construction and selection of the range of polynucleotide sequences within the present claims scope does not require more than routine cloning and screening by, *e.g.*, a BLAST search, against SEQ ID NO:71, 72, or 73, which are among the most basic laboratory procedures. Furthermore, simple plant transformation methods can then be employed to identify functional *DMT* polynucleotides. Such routine screening procedures have never been considered "undue" experimentation by the courts or the Patent Office. In the present case, any desired *DMT* polynucleotide sequence that comprises SEQ ID NO:71, 72, or 73, as recited in the claims, can be obtained from a commercial source or using standard cloning techniques. These nucleic acids can subsequently be tested for activity using the well-established simple methods taught in the specification. Nothing articulated by the Examiner contradicts this clear indication of the

ability of one of skill to readily determine the operability of any potential claimed embodiment. Thus the claims, as pending, are clearly enabled.

The Examiner also questioned the assertion that the claimed *DMT* nucleic acid encodes an endonuclease III or a glycosylase, citing weak sequence homology. Applicants note that sequence homology is not the only basis for the asserted enzymatic function. As the instant specification describes in detail, the structure of full length DMT polypeptide (exemplified by SEQ ID NO:2) shows similarity in various domains (*e.g.*, bipartite nuclear localization signal and leucine zipper) and residues (*e.g.*, K1286 and D1304) associated with the functionality of the enzymes. *See*, page 13 line 14 to page 14 line 13. The totality of these conserved elements of the DMT polypeptides and overall sequence homology supports the conclusion that DMT polypeptides have the asserted enzymatic function. Applicants submit that the Examiner has not carried burden to show why such asserted functionality is not credible. Thus, no enablement rejection should be sustained on this ground.

With regard to the Examiner's assertion that the instant application does not teach methods for assaying protein functions as asserted or methods for transforming plant cells with the claimed nucleic acids, Applicants note that such methods are generally known to those skilled in the art and an ordinarily skilled artisan would not need to rely on the disclosure of the present application to confirm the protein functions as asserted or to perform transformation of plant cells with the claimed nucleic acids. Moreover, the instant specification does provide guidance in how to assay for the asserted protein functions (*see, e.g.*, page 37 line 28 to page 39 line 7, Example 3, and Example 5) or how to transform plant cells with the claimed nucleic acids (*see, e.g.*, page 35 line 4 to page 36 line 24). Thus, Applicants submit the present application does not lack proper enablement for this reason.

Taken together, the above analysis indicates proper enablement of the claimed invention. Applicants thus respectfully request the withdrawal of the enablement rejection.

2. Written Description

Claims 1, 2, 4-8, 13, 15-21, and 24-26 were rejected under 35 U.S.C. §112 first paragraph for alleged inadequate written description. Applicants respectfully traverse the rejection in light of the present amendment.

As amended, the pending claims are drawn to nucleic acids comprising a polynucleotide sequence, or complement thereof, encoding a polypeptide comprising SEQ ID NO:71, 72, or 73 and having one of the recited biological activities. The claims fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Finally, the MPEP states that structural formulas provide a convenient method of demonstrating possession of specific molecules. MPEP §2163.

Claims 1, 13, 15, and 24 (and hence their dependent claims) define the claimed genus of nucleic acids based on a structural feature of the polypeptides they (or their complement) encode, i.e., comprising a defined domain (SEQ ID NO:71, 72, or 73). Such a structural feature of polypeptides is also a structural feature of the encoding nucleic acids, because the amino acid sequence of a polypeptide is dictated by the nucleotide sequence of the nucleic acid encoding the polypeptide. Applicants submit, therefore, that the claimed nucleic acids are thereby defined via shared structural properties.

On the other hand, proper description of functional features of a claimed invention can play an important role in satisfying the written description requirement. The Federal Circuit recently stated that "*Lilly* did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is

sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 USPQ2d 1385, 1398 (Fed. Cir. 2003).

The amended claims also define the claimed genus of nucleic acids based on functional features of the polypeptides they (or their complement) encode, i.e., having at least one of the recited biological activities. The specification further teaches methods for testing such functional features, as discussed in the last section.

Thus, the structural and functional features commonly shared by the claimed genus have been described in detail, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). Such description is consistent with the written description standards set forth in *Lilly* and *Amgen*.

The Examiner asserted that the present disclosure describes only one exemplary sequence (SEQ ID NO:2) and thus would not meet the written description requirement for the scope of the claims. Applicants cannot agree.

First, Applicants note that the sequence listing as filed provides 70 sequences, which represent a large number of sequences encompassed by the pending claims. Second, the Examiner has placed too great an emphasis on the number of representative sequences and overlooked that the specification describes domains (*e.g.*, SEQ ID NO:71, 72, or 73) conserved among a large number of homologous sequences for many plant species. Since these motifs are conserved across plant species, they represent sequences correlating to functions.

Moreover, the domains described in the specification provide guidance to those of skill in the art to identify amino acid residues relevant to function and indicates possible alternatives that maintain function. The Federal Circuit in *Lilly* confirmed that every species in a genus need not be described. It is required, however, that the specification provide "structural features commonly possessed by members of the genus that distinguish them from others" (Emphasis added). *Id.* As stated above, the specification provides structural features of DMT polypeptides that distinguish the polypeptides from others and provides a basis for their function

as required by the Federal Circuit. In criticizing the use of SEQ ID NO:2 as the only example of the claimed genus of nucleic acids, the Examiner took a position that is inconsistent with *Lilly*. By providing structural elements, i.e., the consensus sequences of the conserved domains, the specification provides support for the entire claimed genus, not just the described embodiments. It is unreasonable and also redundant to require Applicants to test every sequence comprising the defined domains.

In summary, the specification provides significant guidance as to which sequences (*e.g.*, SEQ ID NO:71, 72, or 73) are important for function. Multiple exemplary DMT polypeptide sequences are provided in the specification. As such, Applicants submit the written description requirement is met for the full scope of the claims and respectfully request the withdrawal of the rejections under 35 USC §112 first paragraph.

C. 35 U.S.C. §112 Second Paragraph

Claims 4-8, 13, 15-21, and 24-26 were rejected under 35 U.S.C. §112 second paragraph as allegedly indefinite.

Claim 4 was deemed indefinite for its recitation of "a domain of claim 1." Claim 4 has been canceled.

Claim 5 was rejected for its recitation of "meristem stem and/or activity" as well as for parts (a)-(j) not starting with the same part of speech. Claim 5 has been canceled. The basis for this rejection has been addressed to the extent the functional limitations of claim 5 are recited in claims 1, 13, 15, and 24.

Claim 7 was rejected for lack of antecedent basis in claim 1 by reciting "the polynucleotide." As amended, the claim now recites "the polynucleotide sequence," which finds proper antecedent basis in claim 1.

Claim 13 was rejected as the Examiner alleged that "it is not clear to what the polynucleotide sequence is heterologous." Applicants contend that the language "a promoter operably linked to a heterologous polynucleotide sequence" clearly indicates that the promoter and the polynucleotide sequence are "heterologous" to each other. To expedite prosecution,

however, Applicants have amended the claim to recite that "the promoter is heterologous to the polynucleotide sequence." The amendment thus does not alter claim scope. In light of this amendment, Applicants urge that the indefiniteness rejection on this ground be withdrawn.

Claims 13, 15, and 24 were rejected for the phrase "polypeptide of claim 1." As amended, these claims no longer recite this phrase.

Claim 18 was rejected for its recitation of "modulating transcription." The Examiner alleged that "modulating" is indefinite because the term may mean increase or decrease. Applicants agree that, as used in this application, the term "modulating" encompasses both increase and decrease, but do not believe the term is therefore indefinite. The specification provides examples of both increased and decreased transcription.

The Examiner further alleged that it is unclear that the transcription of what gene is "modulated." Applicants note that the claimed genus of *DMT* nucleic acids encode polypeptides capable of general modulation of gene transcription by epigenetic means, *e.g.*, methylation, which is not sequence-specific and thus not limited to any particular gene or genes. The present specification states that DMT regulates gene transcription by a demethylation mechanism and is involved in maintaining the globe pattern of methylation of chromosomal DNA in cells. *See, e.g.*, page 21 lines 24-27. A person of ordinary skill in the art would have no difficulty to understand, especially upon reading the instant disclosure, the metes and bounds of the claims reciting this term. Hence, the recitation of "modulating transcription" should not be deemed indefinite.

In view of the above, Applicants respectfully submit that the indefinite rejections are overcome or moot due to the present amendment.

D. 35 U.S.C. §102

1. Bevan et al. (GenBank Accession Nos. O49498, T05430, and T48453)

Claims 1 and 5-6 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Bevan et al. disclosing GenBank Accession Nos. O49498, T05430, and T48453. Applicants respectfully traverse the rejection in light of the present amendment.

Each of these three nucleic acids encodes a polypeptide with 61-70% identity to SEQ ID NO:71 or 72. Claim 1 (and hence its dependent claims 5 and 6) as amended recites a polypeptide comprising SEQ ID NO:71, 72, or 73. Therefore, the Bevan et al. disclosure cannot anticipate the claims as amended. Applicants thus request the withdrawal of the rejection.

2. *Lin et al. (Sptrembl Accession Nos. Q9SR66 and Q9SJQ6)*

Claims 1, 5, and 6 were rejected under 35 U.S.C. §102(a) as allegedly anticipated by Lin et al. disclosing Sptremble Accession Nos. Q9SR66 and Q9SJQ6. Applicants traverse the rejection in light of the present amendment.

Each of these two nucleic acids encodes a polypeptide with 59-69% identity to SEQ ID NO:71 or 72. As amended, claims 1, 5, and 6 recite a polypeptide comprising SEQ ID NO:71, 72, or 73. Therefore, the claims as amended cannot be anticipated by the Lin et al. disclosure. Applicants thus request the withdrawal of the anticipation rejection.

3. *Bevan et al. (GenBank Accession Nos. T48452, T48453, and T48454)*

Claims 1, 2, 4-7, 15, and 16 were rejected under 35 U.S.C. §102(a) as allegedly anticipated by GenBank Accession Nos. T48452, T48453, and T48454. Applicants respectfully traverse the rejection in light of the present amendment.

These three nucleic acids encode polypeptides with nearly 100% identity to three different segments of SEQ ID NO:2 (1-756, 785-1333, and 1496-1729). These three segments of SEQ ID NO:2, however, comprise none of the entire SEQ ID NO:71 (corresponding to 697-796 of SEQ ID NO:2), SEQ ID NO:72 (corresponding to 1192-1404 of SEQ ID NO:2), or SEQ ID NO:73 (corresponding to 1452-1722 of SEQ ID NO:2). *See*, page 13 lines 3-6 of the specification and alignment results provided by the Examiner. Therefore, the Bevan et al. disclosure cannot anticipate the claims as amended. Applicants thus request the withdrawal of the rejection.

4. Rousley et al. (GenBank Accession Nos. B60854 and B28303)

Claims 1-7, 15, and 16 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Rousley et al. disclosing GenBank Accession Nos. B60854 and B28303. Applicants respectfully traverse the rejection in light of the present amendment.

These two nucleic acids have about 99% identity to different segments of SEQ ID NO:5, as shown in the alignment results (attached as Exhibit A). Upon comparing SEQ ID NO:5 (DMT cDNA sequence) and SEQ ID NO:6 (DMT 5' untranslated region), one can determine that the DMT open reading frame (ORF) starts at nucleotide position 1479 of SEQ ID NO:5. B28303 is nearly identical to the 1122-1605 segment of SEQ ID NO:5, which corresponds to a portion of the 5' untranslated region and the beginning of the DMT ORF--up to the first 42 amino acid residues of SEQ ID NO:2. The complement of B60854 is nearly identical to the 396-895 segment of SEQ ID NO:5, which is entirely within the 5' untranslated region upstream of the DMT ORF. As indicated above, SEQ ID NO:71, 72, and 73 correspond to 697-796, 1192-1404, and 1452-1772 of SEQ ID NO:2, respectively. It is therefore clear that pending claims as amended cannot be anticipated by the Rousley et al. disclosure. Applicants thus request the withdrawal of the rejection.

E. Obviousness-Type Nonstatutory Double Patenting

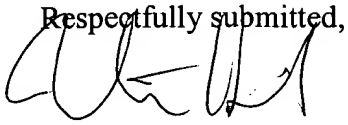
Claims 1-8, 13, 15-21, and 24-26 were rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-38 of U.S. Patent No. 6,476,296. Applicants will gladly consider providing a terminal disclaimer when the Examiner indicates that the claims are otherwise allowable.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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